

Request for Applications Small Clinical Trials Advancing HIV Remission and Cure

The AIDS Clinical Trials Group (ACTG) Network in collaboration with the NIAID Division of AIDS (DAIDS) has developed a new pathway for the conduct of small experimental trials that aim to advance efforts related to HIV remission and cure utilizing the infrastructure of the ACTG Network. It is anticipated these studies will be small (< 30 participants) and will involve 1-3 clinical research sites experienced at these types of trials. The trials will by nature be intensive and may include specialized assays or procedures, thus making them unsuitable for the ACTG's larger multi-site studies. Concepts selected for development will be managed by the ACTG's newly-created Small Clinical Trials Unit (SCTU) with dedicated clinical trial specialists and statistical support. The studies will be conducted at ACTG sites, and the efforts will be coordinated with the ACTG's Reservoirs, Remission, and Cure Transformative Science Group (Cure TSG). This mechanism is open broadly to investigators with interest in experimental science clinical trials addressing questions important to the HIV cure agenda, and proposing investigators do not need to be affiliated with the ACTG.

Successful applicants will work with the ACTG SCTU to finalize protocol development and implementation, which will be overseen by the Cure TSG steering committee. The submitting investigator may serve as the study's chair; additional team members with experience working at ACTG sites will be added to the protocol team. DAIDS will be the sponsor if the study requires an IND/IDE.

To the extent possible, the ACTG will support all primary endpoint laboratory assays in the currently funded specialty laboratories or through contract laboratories. Secondary, exploratory, and specialized assays can be performed by the applicant but will not be routinely funded by the ACTG. This RFA will not fund assay development. Excess samples will be saved in the ACTG specimen repository and will be available to investigators, both internal and external to the ACTG, for work outside the objectives of the original trial via a standard ACTG request and review process.

The ACTG Statistical Data Center (SDAC) will lead the analyses of primary endpoint data. Analyses of secondary and exploratory endpoints will be conducted in collaboration with the proposing investigators' statistical experts and SDAC.

Applications must demonstrate clear linkage to the DAIDS and ACTG scientific agendas. Examples of areas of particular scientific interest to include but are not limited to:

- Quantification and characterization of HIV reservoirs and their decay on current antiretroviral therapy or in response to experimental therapies
- Mechanisms of HIV persistence, immune control and/or immune escape.
- Therapeutic vaccination to enhance immune clearance of HIV-infected cells
- Immune-based therapies to clear virus expressing cells and/or control HIV reservoirs
- Novel therapies to induce HIV expression and deplete HIV reservoirs including combination interventions

Application Procedure

- Applications should use PHS 398 forms and proposal format, except that the Research Plan is limited to 6 pages (single-spaced, 11 pt Times New Roman font). Applicants should include the following information in their proposals:
 - Prior and current experience with specific HIV remission and cure studies and a summary of past contributions to the field of HIV remission and cure.
 - Proposed scientific contributions to the ACTG and DAIDS agendas in the area of HIV cure and remission.
 - NIH-format biosketches for the PI/other key personnel.
 - Other Support for key personnel.
- The grant format should include the following sections:
 - Background
 - Accomplishments
 - Innovation
 - Approach, - should contain the basic design of proposed clinical trial including rationale, hypotheses, objectives and outcomes, study population, intervention and analysis plan
 - Investigators

A schedule of events may be included as the single appendix.

Criteria for Evaluation

Proposals will be evaluated on the basis of significance, originality, feasibility, and likely contribution to the HIV remission/cure agenda of the ACTG and DAIDS.

Specific criteria will include:

- **Investigators:** Are the investigators qualified to design, oversee and perform the proposed work, as judged by past accomplishments (publications; independent peer-reviewed support), and/or patient-oriented AIDS research, and experience working in regulated environment? Access to trainees and junior faculty as collaborators in the work should also be described.
- **Institutional Resources:** Does the investigator have the resources and environment to conduct assays that will be done outside of the ACTG specialty or contract labs and participate in the statistical analysis? If the applicant proposes to utilize a non-ACTG laboratory, does the team have the capabilities and resources to meet ACTG standards (e.g. QA/QC, data management) and perform any specialized assays required by the concept proposal? Is the host institution committed to providing the necessary space and other infrastructure needed to complete the required work for the duration of the award?
- **Innovation:** Will the study, if successful, advance efforts to understand HIV reservoirs and/or facilitate HIV remission/cure?

- Approach: Does the concept propose a study focused on an area of scientific interest to the field of HIV reservoirs and/or HIV remission that is investigational and intensive, uses non-standard experimental endpoints, and/or requires specialized assays or procedures, thus making it unsuitable for the ACTG's larger multi-site studies? If the study requires experimental interventions or devices, are they available to the investigator?

Application Timelines

This RFA has twice-yearly receipt dates on March 1st and September 1st.

An optional Letter of Intent may be submitted by August 1st and April 1st that includes the principal investigator, other key investigators, investigator institution, tentative title of the proposal, primary hypotheses and intention to conduct specialized laboratory assays outside of the ACTG and contract laboratories.

Release of solicitation: July 12, 2021

First application due date: September 1, 2021

EXPECTED SUPPORT OF FUNDED APPLICATIONS

1. The funded applications will generally receive an award of 3 years duration.
2. The ACTG intends to fund up to 2 small clinical trial awards per year.
3. The ACTG will provide protocol development support, clinical trials expertise, regulatory support, statistical and data support and the sites, staff and laboratory support need to conduct the trial.
4. Primary and secondary endpoint assays conducted by the ACTG specialty labs or contract labs will be supported by the ACTG.
5. Each awardee will receive core support of up to 25% FTE up to the NIH salary cap per year, direct costs. (This funding is to support the effort of the PI and other Key Personnel who will be directly involved in the development and conduct of the clinical trial and will be provided as part of protocol development and implementation as per ACTG standard operating procedures.)
6. Assay performance work that is deemed essential to the trial and conducted outside of the ACTG or contract labs may be supported by the ACTG using a cost-reimbursement model, depending on the nature of the assays and the volume of work required.
7. Support for exploratory assays is the responsibility of the proposing investigators.

Application Submission and Questions

Completed applications are to be submitted on or after August 15, 2021 to a portal available at: <https://actgnetwork.org/submit-a-proposal/>.

Questions about the RFA can be sent to ACTGLeadershipSupport@DLHCorp.com; an F&Q will be developed and posted to the same portal.